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KAREN GUERRERO
25 ROOSTER HILL RD
PHOENIXVILLE, PA 19460

EXAMINER	
ROYDS, LESLIE A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/992,235	LEDERMAN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,25-27,30,31 and 36-39* is/are pending in the application.

4a) Of the above claim(s) *25-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,30-31,36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8, 25-27, 30-31 and 36-39 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 114. Applicant's payment and submission filed December 18, 2009 have been received and entered into the present application. Accordingly, prosecution has been reopened.

Claims 1-8, 25-27, 30-31 and 36-39 are pending. Claims 25-27 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b). Claims 36-39 are newly added. Claims 32-35 is cancelled. Claims 1 and 30 are amended. Claims 1-8, 30-31 and 36-39 are under examination.

Applicant's arguments, filed December 18, 2009, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Compliance with the Requirements of 37 C.F.R. 1.111

Applicant is reminded of the requirements of 37 C.F.R. 1.111(b), which specifically states that the reply by the Applicant or patent owner must be reduced to writing which distinctly and specifically points out the supposed errors in the examiner's action and must reply to every ground of objection and rejection in the prior Office action. Applicant's repeated submissions of remarks that generally address the rejections of record without specifically delineating to which rejections they are intended to apply is not consistent with the provisions of 37 C.F.R. 1.111. Applicant's remarks will be herein addressed as completely as possible and will be considered in the context of the rejection to which they appear to most

appropriately apply. Applicant is reminded of the guidance provided in 37 C.F.R. 1.111 regarding the requirements for a proper reply to an outstanding Office Action and is notified that subsequent submissions with this same deficiency may be held non-compliant.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement, New Matter (New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 30-31 and 36-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In particular, the specification and claims as originally filed fail to provide adequate written description for the newly added limitation directed to (1) the effective amount of the claimed pharmaceutical composition between 0.7 mg/ml and 1.3 mg/ml (claims 1 and 30), (2) the administration of the composition at a dosage that is between 0.8 mg/kg and 1.2 mg/kg (claims 36 and 38), or (3) the administration of the composition at a dosage that is between 0.9 mg/kg and 1.1 mg/kg (claims 37 and 39).

Applicant generally directs the Examiner to the disclosure found in Example 4 (p.27-34) and the Figures associated with this example (i.e., in particular, Figures 3C and 7C) as implicitly supporting the concept that Applicant envisioned using (R,R'),(R,S')-amphetaminil at dosages of about 1 mg/kg rather than only at a dosage of 1 mg/kg. Specifically, Applicant contends that Figures 3C and 7C show dose response curves for (R,R'),(R,S')-amphetaminil showing changes in locomotor activity (Figure 3C) and

stereotypy (Figure 7C) and, therefore, allegedly show implicit support for dosages between 0.7 mg/kg to 1.3 mg/kg, between 0.8 mg/kg to 1.2 mg/kg and between 0.9 to 1.1 mg/kg, which Applicant asserts provide the unexpected results of the instant invention.

Example 4 is directed to a study of amphetaminil sulfate, amphetamine and fusaric acid on locomotor activity and induction of stereotyped behavior in normal rats. Specifically, the disclosure states, "Male Wistar rats (n=4 per group) were randomly allocated to each drug treatment group. Drugs were administered such that, with the exception of fusaric acid, each rat in each group received all doses of the drug or vehicle in a semi random manner according to the modified Latin Square in Table 1. Compounds were administered at the doses: 0.1, 1 and 10 mg/kg s.c. in 100% DMSO (vehicle). Amphetamine was administered at 0.1, 1 and 5 mg/kg s.c. in saline (vehicle). Fusaric acid was administered at 20, 40 and 80 mg/kg s.c. in saline (vehicle). Rats received each dose of fusaric acid (20, 40 and 80 mg/kg), doses given in order, starting with vehicle. A one-week interval was provided between doses." (para. bridging p.27-28).

Figures 3C presents a sigmoidal dose response curve of (R,R'),(R,S')-amphetaminil based upon the study of locomotor activity in rats administered the amphetaminil compound in amounts of 0.1 mg/kg, 1 mg/kg and 10 mg/kg as studied in Example 4. Figure 7C presents a sigmoidal dose response curve of (R,R'),(R,S')-amphetaminil based upon the study of stereotyped behavior in rats administered the amphetaminil compound in amounts of 0.1 mg/kg, 1 mg/kg and 10 mg/kg.

However, the disclosure of the administration of the instantly claimed compound (R,R'),(R,S')-amphetaminil in amounts of 0.1 mg/kg, 1 mg/kg and 10 mg/kg s.c. in 100% DMSO vehicle fails to provide adequate written support to now broaden the claims to read upon a specific effective amount in the range of (1) between 0.7 mg/ml to 1.3 mg/ml (claim 1), (2) between 0.8 mg/kg and 1.2 mg/kg (claims 36 and 38) or (3) between 0.9 mg/kg and 1.1 mg/kg (claims 37 and 39). This is a concept that is not adequately supported by the written description of the invention as provided in the specification and

claims as originally filed because the disclosure of "0.1 mg/kg", "1 mg/kg" or "10 mg/kg" does not provide adequate support to then broaden the claims to read upon the use of the same compound in a range that is neither described explicitly nor implicitly in the disclosure as originally filed.

With regard to Applicant's newly added limitation to instant claim 1 (i.e., an effective amount between 0.7 mg/ml and 1.3 mg/ml), not only does the specification and claims as originally filed fail to set forth any range of values in mg/ml concentration, it also does not even specifically describe any concentration of the instantly claimed compound in a range of 0.7-1.3 of *any* measurable unit. This newly added limitation represents a clear broadening of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure and clearly circumscribes a concept that was not in Applicant's possession at the time of the invention.

In addition, with regard to Applicant's newly added limitations to instant claims 36-39 (i.e., administration of the composition in an amount between 0.8 mg/kg and 1.2 mg/kg as recited in instant claims 36 and 38 or administration of the composition in an amount between 0.9 mg/kg and 1.1 mg/kg as recited in instant claims 37 and 39), the specification and claims as originally filed fail to set forth any range of values in and around the individually described amounts of 0.1 mg/kg, 1 mg/kg or 10 mg/kg. In other words, there is no disclosure in the specification or claims as originally filed that supports the idea that Applicant was in possession of the instantly claimed composition in amounts that vary around each of these individually described amounts. These newly added limitations represent a clear broadening of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure and clearly circumscribe a concept that was not in Applicant's possession at the time of the invention.

Moreover, Applicant attempt to rely upon the disclosure found in Example 4 and Figures 3C and 7C to support this newly added limitation (i.e., "between 0.7 mg/ml to 1.3 mg/ml") is unpersuasive in

establishing this newly added range as being within Applicant's possession at the time of the invention. Specifically, Applicant alleges that the figures show implicit support for the newly claimed range because the data is presented in the form of a dose response curve across a range of values. However, this argument is clearly unimpressive in establishing conception of this newly added range because both Figures 3C and 7C are each directed to amounts of amphetaminil in mg/kg amounts, *not* mg/ml amounts as instantly claimed.

That being said, the dose response curves still fail to establish that Applicant was in possession of any other amounts (such as those now claimed in instant claims 36-39) aside from the three particular amounts of amphetaminil studied (i.e., 0.1 mg/kg, 1 mg/kg and 10 mg/kg). This is because it is clear from the accompanying description of the Figures that the only dosage amounts contemplated and employed by Applicant were 0.1 mg/kg, 1 mg/kg and 10 mg/kg, not amounts "around" or "about" each of these values. Though it is agreed that the Figures present the data as a continuous line graph, it is noted for the record that this is an attempt to extrapolate the results beyond those data points actually conceived of and tested (i.e., 0.1 mg/kg, 1 mg/kg and 10 mg/kg) and does not either explicitly or implicitly demonstrate that Applicant contemplated or conceived of a composition of the claimed compound that was capable of achieving the claimed result at any other dosage amounts other than those explicitly described (i.e., specifically, at a dose of 1 mg/kg). Furthermore, note that, even if the dose response curve did suggest values in and around the amounts specifically studied (which the Examiner does not concede), the newly added range represents a subgenus of values that was not previously set forth or described or would have been immediately envisaged by one of ordinary skill in the art from the specification as originally filed. Once again, Applicant's amendment attempts to broaden the subject matter originally described and claimed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure.

As stated in MPEP §2163, "The subject matter of the claim need not be described literally (i.e., using the same terms of *in haec verba*) in order for the disclosure to satisfy the description requirement." However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the concepts of (1) the effective amount of the claimed pharmaceutical composition between 0.7 mg/ml and 1.3 mg/ml (claims 1 and 30), (2) the administration of the composition at a dosage that is between 0.8 mg/kg and 1.2 mg/kg (claims 36 and 38), or (3) the administration of the composition at a dosage that is between 0.9 mg/kg and 1.1 mg/kg (claims 37 and 39).

Accordingly, the claims are considered to lack sufficient written description and are properly rejected under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 30-31 and 36-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salvesen et al. ("NMR and ORD Determination of the Configuration of the N-Cyanobenzylamphetamine (AN 1)", *Aezneim-Forsch. (Drug Res.)*, 1974; 24(2):137-140), in light of STN Registry File No. 17590-01-1 ("Amphetaminil", 2008) and Stedman's Medical Dictionary (Twenty-Second Edition, 1972; p.377), each cited to show facts, in view of Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; p.420-425), each already of record, for the reasons of record set forth at p.5-8 of the previous Office Action dated September 21, 2009, of which said reasons are herein incorporated by reference.

Newly amended claims 1 and 30 and newly added claims 36-39 are properly included in the instant rejection because the determination of the optimal dosage amount would have been a matter well within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not been limited to, the age, body weight, symptoms, desired therapeutic effect, route of administration, duration of treatment, etc. Other factors that would have been considered would have included the sex, diet and medical condition of the patient, severity of the disease, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination, among others. Thus, the dosage amount of the instantly claimed composition that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed, absent factual evidence to the contrary.

Response to Applicant's Arguments

Applicant fails to provide any specific remarks directed to the instant rejection under 35 U.S.C. 103(a). However, it is understood that the amendments to instant claims 1 and 30 and newly added claims 36-39 to require an amount of the instantly claimed compound that is believed by Applicant to be "about 1 mg/kg" is an attempt to obviate the instant rejection by amending the claims to apparently be commensurate with the unexpected results.

However, the amendments do not overcome the instant finding of obviousness. Though it is presumed that Applicant's amendment was made in an attempt to limit the instant claims to a therapeutically effective amount of "about 1 mg/kg" for which Applicant appears to have demonstrated an unexpected effect over the cited prior art, the claims now recite a range of concentrations (i.e., "between 0.7 to 1.3 mg/ml", "between 0.8 mg/kg to 1.2 mg/kg" or "between 0.9 mg/kg to 1.1 mg/kg") of amphetaminil for which Applicant has failed to provide any evidence of unexpected activity so as to support his contention that the instantly claimed invention distinguishes over the cited prior art. The sole embodiment of the instantly claimed composition for which Applicant has demonstrated an unexpectedly greater effect is 1 mg/kg of the claimed composition in 100% DMSO vehicle. The fact that the instant claims continue to circumscribe embodiments of the invention that were not shown to demonstrate activity that was unexpectedly greater than what would have been predicted from the prior art is a clear indication that the finding of obviousness remains proper because the claims are not so limited to those particular embodiments for which Applicant has provided evidence of unexpected activity.

These facts, coupled with the fact that Applicant's failure to amend the claims to specify the particular vehicle used to elicit the unexpected results (i.e., 100% DMSO vehicle), clearly support the fact that the instant claims are still not limited to the particular embodiment(s) that were demonstrated as being unexpected. Applicant is again reminded that should he rely upon unexpected results to patentably distinguish over the prior art, the present claims must be limited to the embodiment(s) which is (are), in

fact, unexpected. Note also that Applicant is burdened with the responsibility of explaining why the evidence provided to support secondary considerations is probative of non-obviousness beyond what data is explicitly provided as unexpected. Please see MPEP §716.02(b)[R-2], particularly Section (II), which states, "[A]ppellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness." *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. &. Inter. 1992). In the instant case, though the instant data was provided in the accompanying specification and not a declaration, the burden is nonetheless on Applicant to explain the data provided as evidence of non-obviousness of the claimed subject matter.

In view of the reasons provided *supra*, the evidence supporting the obviousness of the instantly claimed invention outweighs the remarks and amendments provided to support the non-obviousness of the instantly claimed invention. The rejection, therefore, stands.

For these reasons *supra*, and those previously made of record at p.5-8 of the Office Action dated September 21, 2009, rejection of claims 1-8, 30-31 and 36-39 is proper.

Conclusion

Rejection of claims 1-8, 30-31 and 36-39 is proper.

Claims 25-27 remain withdrawn from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

January 07, 2010